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EXAMINER	
HUI, SAN MING R	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 11/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/982,554	ZOHOUNGBOGBO, MATHIAS C.	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments filed August 18, 2004 have been entered. The cancellation of claims 27-39 and 41-44 is acknowledged. The addition of claims 45-56 is acknowledged. Claims 45-56 are pending.

The outstanding rejections under 35 USC 112, first and second paragraph are withdrawn.

Examiner notes that the dosage of metformin recited in the claims is apparently very high. The minimal dosage of metformin recited in claims 50, for example, 36% of 7g equals to around 2550mg, which is the maximum dosage of metformin. For the high end of metformin dosage, 41% of 23g is around 9g of metformin, is very high and probably would cause a potentially fatal condition, lactic acidosis. Therefore, such high dose of metformin may not be enabled in the instant specification. Appropriate correction is recommended.

Claim Objections

Claim 56 is objected to because of the following informalities: in line 4, "determining is said person is suffering from ..." "if" apparently misspelled as "is". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any

> person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 48, 49, 53, and 54 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The limitations with regard to the weight ratio of selenium: "0.09:1 to 0.3:1", that of yohimibine: "0.0009:1 to 0.0007:1", that of phendimetrazine pamoate: "0.004:1 to 0.13:1", that of vitamin A: "0.5:1 to 1.8:1", that of vitamin B1: "0.002:1 to 0.2:1", that of vitamin B6: "0.05:1 to 0.2:1", that of dipotassium cholorazepate: "0.0005:1 to 0.03:1", that of anoretic agent: "0.002:1 to 1.3:1", and that of triiodiotiroacetic acid: "0.0002:1 to 0.003:1" are not supported by the originally filed specification and originally filed claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 56 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 56 recites the limitation "the weight loss method" in last line. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 45, 47, 49-50, 52, and 54 -56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Marquie et al. (Life Sciences,1998; 63(1):65-76), Pentikainen et al. (Annals of Medicine, 1990 ;22 :307-312), and Poupon et al. (Hepatology, 1993; 17(4): 577-582) in view of Spasmo-canulase® Bitab® package insert (July 1989), references of record and Krause et al., (Food, Nutrition, and Therapy, 7th ed., 1984, page 656-658, W.B. Saunders Company).

Marquie et al. teaches benfluorex as useful in treating hypercholesterolemia (See abstract, also page74, whole page).

Pentikain et al. teaches the cholesterol lowering affect of metformin (See the abstract, also page 309, Table 2).

Poupon et al. teaches ursodesoxycholic acid as useful in lowering hypercholesterolemia (See particularly the abstract).

The references do not expressly teach the method of treating the side effects of a ketogenic diet with the combination of benfluorex, metformin and ursodesoxycholic acid. The references do not expressly teach the herein claimed amount ratio employed. The references do not expressly teach the employment of pancreatin and sodium dehydrocholate with benfluorex and metformin. The references do not expressly teach the dosage of the composition herein claimed as 7g to 23g. The references do not expressly teach the method further include steps that replace the food composition in form of a flour having no more than 20% carbohydrates by weight and determine the patients whether is suffering from the side effects of ketogenic diet.

Spasmo-canulase® Bitab® package insert teaches Spasmo-canulase® Bitab®, which contains pancreatin and sodium dehydrocholate, is useful in treating abdominal camps associated with flatulence.

Krause et al. teaches ketogenic diet as approximately 90% of calories are from fat and only around 11% of calories are from proteins and carbohydrates (page 657, col. 1-2).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to treat side effects of a ketogenic diet (hypercholesterolemia being one of the side effects of ketogenic diet) with the combination of benfluorex, metformin and ursodesoxycholic acid. It would have been obvious to one of ordinary skill in the art at the time the invention was made

to incorporate pancreatin and sodium dehydrocholate in the treatment method herein. It would have been obvious to one of ordinary skill in the art at the time the invention was made to include steps that replace the food composition in form of a flour having no more than 20% carbohydrates by weight and determine the patients whether is suffering from the side effects of ketogenic diet.

One of ordinary skill in the art would have been motivated to treat side effects of a ketogenic diet (hypercholesterolemia being one of the side effects of ketogenic diet) with the combination of benfluorex, metformin and ursodesoxycholic acid. Combining and employing two or more agents which are known to be useful to lowering hypercholesterolemia individually into a single method useful for the very same purpose (treating hypercholesterolemia) is prima facie obvious. See *In re Kerkhoven* 205 USPQ 1069. One of ordinary skill in the art would have been motivated to incorporate pancreatin and sodium dehydrocholate in the treatment method herein because Spasmo-canulase® Bitab®, which contains pancreatin and sodium dehydrocholate, is known for relieving abdominal cramps associated with flatulence. Since flatulence and abdominal cramps are the common side effects of metformin, employing Spasmo-canulase® Bitab® would be reasonably expected to be effective in relieving the side effects of metformin and be useful in the herein claimed method, which utilize metformin. Furthermore, the optimization of result effect parameters (i.e., dosage range, dosing regimens) is obvious as being within the skill of the artisan.

One of ordinary skill in the art would have been motivated to include steps that replace the food composition in form of a flour having no more than 20% carbohydrates by weight and determine the patients whether is suffering from the side effects of ketogenic diet. Since ketogenic diet is known to have a certain portion of carbohydrate, fats and proteins, then adjusting the amounts of each to fit individual needs would be considered obvious as being within the purview of skilled artisan. Monitoring (determining) whether the patients still have the side effects or not is an integral part of therapy, which is obvious within the purview of the skilled artisan.

Claims 46 and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Marquie et al., Pentikainen et al., Poupon et al., Spasmo-canulase® Bitab®, and Krause et al. package insert as applied to claims 45, 47, 49-50, 52, and 54 -56 above, and further in view of Hydrocotyle (A Modern Herbal Home Page, 1995), Kang et al. (Archives of Physiology and Biochemistry, 1997;105(6):603-607), Pondimin monograph (PDR, 1996, page 2066-2067), and Keown et al. (WO 95/11034), references of record.

Marquie et al., Pentikainen et al., Poupon et al., and Spasmo-canulase® Bitab® package insert suggest the method of treating side effects of ketogenic diet by employing the herein claimed agents.

The references do not expressly teach the ketogenic diet side effects treating method employing also centella asiatica triterpene, selenium, yohimbine, phendimetrazine, and fenfluramine in the herein claimed amount.

Hydrocotyle teaches that centella asiatica is known to be a mild stimulant (See the Medicinal Action and Uses Section).

Kang et al. teaches that selenium is useful as lowering cholesterol level in subject taking high fat diet (See the abstract).

Pondimin monograph teaches fenfluramine is useful in increasing glucose utilization (see pharmacology Section).

Keown et al. teaches sympathomimetic agents, such as yohimbine and phendimetrazine, as useful in increasing fat metabolism and lowering serum cholesterol level in the amount from about 0.001 to 99.90% (See particularly page 9, lines 8-16; also claim 5).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ all the herein claimed agents, in the herein claimed amount, into the method of treating the side effects of ketogenic diet.

One of ordinary skill in the art would have been motivated to employ all the herein claimed agents, in the herein claimed amount, into the method of treating the side effects of ketogenic diet. All the agents herein can help relieving one of the side effects of ketogenic diet: centella asiatica, which contains the triterpene, can be useful to treat fatigue since it is a mild stimulant; selenium is useful in treating hypercholesterolemia because it can lower the cholesterol level; fenfluramine is useful for hyperglycemia because it can increase the utilization of glucose and causing hypoglycemia; yohimbine and phendimetrazine are useful for hypercholesterolemia. One of ordinary skill in the art would known that side effects of ketogenic diets include hypercholesterolemia, hyperglycemia,

hyperuricemia, fatigue, change in mental status, nausea, and vomiting. Therefore, combining and employing two or more agents which are known to be useful to treat side effects of ketogenic diet individually into a single method useful for the very same purpose is prima facie obvious. See *In re Kerkhoven* 205 USPQ 1069. Furthermore, the optimization of result effect parameters (i.e., dosage range, dosing regimens) is obvious as being within the skill of the artisan.

Response to Arguments

Applicant's arguments filed August 18, 2004 averring the agents selected herein as intended to be used for treatment of side effects of ketogenic diet, not interfering with the effectiveness of one another have been fully considered but they are not persuasive. Examiner notes that the herein claims are directed to a method of treating side effects of ketogenic diet employing the herein claimed agents without specifying the function of each individual agents. Therefore, possessing the teachings of the cited prior arts, one of ordinary skill in the arts would have been motivated to employ the herein claimed agents in a method to treat side effects of ketogenic diet.

Applicant's arguments filed August 18, 2004 averring the cited prior art's failure to teach the specific intended functions of the herein claimed agents have been considered but they are not persuasive. The arguments are directed to unclaimed limitations. Unclaimed limitations are considered moot. The cited prior arts, when taken together, do suggest the incorporation of the herein

claimed agents be employed in the method of treating the side effects of ketogenic diet.

Applicant's arguments filed August 18, 2004 averring the cited prior arts' failure to combine the agents taught in the cited prior arts have been considered, but are not found persuasive. The herein claimed agents, except for Spasmo-canulase® Bitab®, are known to be useful in treating various side effects of ketogenic diet. Therefore, employing them together for the very same purpose, i.e., treating side effects of ketogenic diet, is considered obvious (See *In re Kerkhoven* supra). Furthermore, Spasmo-canulase® Bitab®, which contains pancreatin and sodium dehydrocholate, is known for relieving abdominal cramps associated with flatulence. Since flatulence and abdominal cramps are the common side effects of metformin, employing Spasmo-canulase® Bitab® would be reasonably expected to be effective in relieving the side effects of metformin and be useful in the herein claimed method, which utilize metformin.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory

action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (571) 272-0626. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

San-ming Hui
Primary Examiner
Art Unit 1617